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Automatic detection of vascular bifurcations in segmented retinal images using trainable COSFIRE filters

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ABSTRACT

Background: The vascular tree observed in a retinal fundus image can provide clues for cardiovascular diseases. Its analysis requires the identification of vessel bifurcations and crossovers.

Methods: We use a set of trainable keypoint detectors that we call Combination Of Shifted Filter Responses or COSFIRE filters to automatically detect vascular bifurcations in segmented retinal images. We configure a set of COSFIRE filters that are selective for a number of prototype bifurcations and demonstrate that such filters can be effectively used to detect bifurcations that are similar to the prototypical ones. The automatic configuration of such a filter selects given channels of a bank of Gabor filters and determines certain blur and shift parameters. The response of a COSFIRE filter is computed as the weighted geometric mean of the blurred and shifted responses of the selected Gabor filters. The COSFIRE approach is inspired by the function of a specific type of shape-selective neuron in area V4 of visual cortex.

Results: We ran experiments on three data sets and achieved the following results: (a) a recall of 97.88% at precision of 96.94% on 40 manually segmented images provided in the DRIVE data set, (b) a recall of 97.32% at precision of 96.04% on 20 manually segmented images provided in the STARE data set, and (c) a recall of 97.02% at precision of 96.53% on a set of 10 automatically segmented images obtained from images in the DRIVE data set.

Conclusions: The COSFIRE filters that we use are conceptually simple and easy to implement: the filter output is computed as the weighted geometric mean of blurred and shifted Gabor filter responses. They are versatile keypoint detectors as they can be configured with any given local contour pattern and are subsequently able to detect the same and similar patterns.

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1. Introduction

Retinal fundus images provide a unique possibility to take a non-invasive look at the eye and the systemic status of the human body. Besides ocular diseases, such as age-related macular degeneration and glaucoma that are two of the leading causes of blindness, other systemic diseases are also manifested in the retina. Complications of such diseases include diabetic retinopathy from diabetes mellitus (Frank, 2004), hypertension (Tso and Jampol, 1982) and atherosclerosis from cardiovascular disease (Chapman et al., 2002), as well as brain diseases and neuropathies, such as multiple sclerosis (Parisi et al., 1999) and Huntington's disease (Paulus et al., 1993). The retina can thus be considered as a mirror of the health status of a person.

Here we focus on retinal image analysis for the diagnosis of cardiovascular diseases, while for a comprehensive review on retinal

image analysis we refer to Abramoff et al. (2010). The vascular geometrical structure in the retina is known to conform to structural principles that are related to certain physical properties (Zamir et al., 1979; Sherman, 1981). For instance, the studies of Murray (1926a,b) revealed that the most efficient blood circulation is achieved when the blood flow is proportional to the cubed power of the vessel's radius; this is known as Murray's law. The branching angle between the two child vessels is also important to optimize the efficiency of the entire vascular network (Zamir et al., 1992).

The analysis of the geometrical structure of the vessel tree is thus important as deviations from the optimal principles may indicate (increased risk of) signs for vascular pathology; a thorough review is given by Patton et al. (2006). The detection of junctions in the vessel tree of a retinal fundus image, commonly referred to as vascular bifurcations and crossovers, is one of the basic steps in this analysis, and it is typically carried out in a time-consuming manual procedure (Chapman et al., 2002). The automation of such a tedious process is thus important to improve the efficiency and to avoid inaccuracies due to human fatigue.

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The existing attempts to automate the detection of retinal vascular bifurcations can be categorized into two classes; geometrical-feature based and model based approaches. The former methods are highly dependent on the segmentation and skeletonization techniques. They also involve extensive local pixel processing and branch point analysis (Martinez-Perez et al., 2002; Chanwimaluang and Guoliang, 2003; Eunhwa and Kyungho, 2006; Bhuiyan et al., 2007; Ardizzone et al., 2008; Aibinu et al., 2010; Calvo et al., 2011). Incomplete bifurcations, which are commonly produced by automatic segmentation techniques, are generally not detected by such skeleton based approaches. On the other hand, model-based approaches are usually more adaptive and have smaller computational complexity that makes them more appropriate for real-time applications (Ali et al., 1999; Shen et al., 2001; Tsai et al., 2004). However, model based approaches suffer from insufficient generalization ability as they are usually unable to model all the features of interest. Consequently, these methods may fail to detect atypical bifurcations.

Besides the diagnosis of pathologies, retinal fundus images have also been used for person verification as the geometrical arrangement of the vascular bifurcations is an effective biometric (Bevilacqua et al., 2009; Ortega et al., 2009). Moreover, vascular bifurcations may also be used as key features to find correspondences between the retinal images of the same eye taken from different views, i.e. for registration of retinal images (Becker et al., 1998; Shen et al., 2003; Tsai et al., 2004; Chen et al., 2011).

We use the COSFIRE (Combination Of Shifted Filter Responses) filters, which we have introduced elsewhere (Azzopardi et al., 2012a), for the detection of bifurcations in segmented retinal images. COSFIRE filters are trainable keypoint detection operators, which are selective for given local patterns that consist of combinations of contour segments. These operators are inspired by the properties of some neurons in area V4 of visual cortex, which are selective for parts of (curved) contours or for combinations of line segments (Pasupathy and Connor, 1999, 2002). In this work we focus on one application and provide more elaborate experiments to demonstrate the robustness and generalization capability of the COSFIRE filters.

The response of a COSFIRE filter in a given point is computed as a function of the shifted responses of simpler filters. Using shifted responses of simpler filters – Gabor filters in the concerned application – corresponds to combining their respective supports at different locations to obtain a more sophisticated filter with a bigger support. The specific function that we use here to combine the responses of simpler filters is weighted geometric mean, essentially multiplication, which has specific advantages regarding shape recognition.

Two-dimensional (2D) Gabor filters (Daugman et al., 1985) that we use as input to our COSFIRE filters have been extensively used to detect oriented structures (lines and/or edges) in many computer vision applications, including retinal image analysis. For instance, these filters have been found effective in detecting signs of glaucoma (Bodis-Wollner and Brannan, 1997; Sun et al., 2006; Muramatsu et al., 2009) detecting the optic nerve head of the retina (Rangayyan et al., 2010), and mostly for the segmentation of the vessel tree in retinal fundus images (Soares et al., 2006; Li, 2006; Usman Akram et al., 2009; Moin et al., 2010; Xiaojun Du et al., 2010; Yavuz et al., 2010, 2011; Fraz et al., 2011; Selvathi et al., 2011). Apart from Gabor filters, other state-of-the-art methods have also been found effective for the segmentation of the vessel tree (Chauduri et al., 1989; Jiang and Mojon, 2003; Staal et al., 2004; Niemeijer et al., 2004; Mendonca and Campilho, 2006; Ricci and Perfetti, 2007).

The rest of the paper is organized as follows: In Section 2 we present our method and demonstrate how it can be used to detect retinal vessel features. In Section 3, we evaluate the effectiveness of the COSFIRE filters on manually and automatically segmented

retinal images from the DRIVE and STARE data sets. In Section 4 we provide a discussion of some aspects of our approach and finally we draw conclusions in Section 5.

2. Method

A COSFIRE filter for the detection of local combinations of lines is conceptually simple and straightforward to implement: it requires the application of selected Gabor filters, blurring of their responses, shifting the blurred responses by specific, different vectors, and multiplying the shifted responses. The questions of which Gabor filters to use, how much to blur them and how far to shift them are answered in a filter configuration process in which a local pattern of interest that defines a keypoint is automatically analyzed. The configured COSFIRE filter can then detect the same and similar patterns.

2.1. Overview

In Fig. 1a we illustrate a typical vascular bifurcation encircled in a segmented retinal fundus image.¹ We use this feature as a prototype bifurcation, which is shown enlarged in Fig. 1b, to automatically configure a COSFIRE filter that will respond to the same and similar bifurcations.

The three ellipses shown in Fig. 1b represent the dominant orientations in the neighborhood of the specified point of interest. We detect such orientations by Gabor filters. The central circle represents the overlapping support of a group of such filters. The response of a COSFIRE filter is computed by combining the responses of the concerned Gabor filters by a weighted geometric mean. The preferred orientations of these filters and the locations at which we take their responses are determined by automatically analyzing the local prototype pattern used for the configuration of the concerned COSFIRE filter. Consequently, the COSFIRE filter is selective for the presented local spatial arrangement of lines of specific orientations and widths. Taking the responses of Gabor filters at different locations around a point can be implemented by shifting the responses of these Gabor filters by different vectors before using them for the pixel-wise evaluation of a function which gives the COSFIRE filter output.

Such a design is inspired by electrophysiological evidence that some neurons in area V4 of visual cortex are selective for moderately complex stimuli, such as curvatures, that receive inputs from a group of orientation-selective cells in areas V1 and V2 (Pasupathy and Connor, 1999, 2001, 2002). Moreover, in a psychophysical experiment, Gheorghiu and Kingdom, 2009 show that curved contour parts are likely detected by a nonlinear operation that combines the responses of afferent orientation-selective filters by multiplication. Since a COSFIRE filter makes use of such multiplication, it produces a response only when all its afferent inputs from Gabor filters are stimulated; i.e. all constituent parts (in this case lines) of a vascular bifurcation are present.

In the following sections we explain the automatic configuration process of a COSFIRE filter that will be selective for the prototype bifurcation shown in Fig. 1b. The configuration process determines which responses of which Gabor filters in which locations need to be combined in order to obtain the output of the filter.

2.2. Detection of dominant orientations by 2D Gabor filters

We build the COSFIRE filter using as input the responses of 2D Gabor filters, which are known to serve as line and edge detectors.

¹ The image used in this example is named 40_manual1.gif in the DRIVE data set (Staal et al., 2004).

Fig. 1. (a) The circle indicates a bifurcation that is selected by a user. (b) Enlargement of the selected feature. The ellipses represent the dominant orientations around the specified point of interest that is indicated by a cross marker.

We denote by $h_{\lambda,\theta}(x,y)$ a Gabor function of preferred wavelength λ and orientation θ :

$$h_{\lambda,\theta}(x,y) = \exp\left(-\frac{x'^2 + \gamma^2 y'^2}{2\sigma^2}\right) \cos\left(2\pi\frac{x'}{\lambda} + \zeta\right), \quad (1)$$

$$x' = x \cos \theta + y \sin \theta, \quad y' = -x \sin \theta + y \cos \theta$$

where γ represents the aspect ratio that specifies the ellipticity of the support of the Gabor function, σ is the standard deviation of the Gaussian envelope and ζ is the phase offset of the sinusoidal wave function. Here, we set $\gamma = 0.5$, as suggested by Petkov (1995), and we set the other parameters to $\sigma = 0.31\lambda$ and $\zeta = 0$.

We denote by $g_{\lambda,\theta}(x,y)$ the response² of a symmetric Gabor filter to a given grayscale image I :

$$g_{\lambda,\theta}(x,y) = I * h_{\lambda,\theta}(x,y) \quad (2)$$

The responses of a symmetrical ($\zeta \in \{0, \pi\}$) and an antisymmetrical ($\zeta \in \{\frac{\pi}{2}, \frac{3\pi}{2}\}$) Gabor filter can be combined in a quadrature filter, commonly referred to as Gabor energy filter. Moreover, surround suppression can be applied as a post-processing step to Gabor (energy) filter responses to reduce responses to texture and improve the detection of object contours. For brevity of presentation we do not consider all these aspects of Gabor filters here and we refer to Petkov and Kruizinga (1997), Kruizinga and Petkov (1999), Grigorescu et al. (2002, 2003a,b), Petkov and Westenberg (2003) for technical details and to our online implementation.³

We re-normalize all Gabor functions that we use in such a way that all positive values of such a function sum up to 1 while all negative values sum up to -1 . Among other things, this ensures that the response to a line of width w will be largest for a symmetrical filter of preferred wavelength $\lambda = 2w$. It also ensures that the response to an image of constant intensity is 0. Without re-normalization, this is true only for antisymmetrical filters. For the specific application at hand, we use symmetrical Gabor functions ($\zeta = 0$) as they respond best to line structures which makes them appropriate to detect the presence of vessels in retinal fundus images.

Fig. 2 illustrates the area of support of a symmetrical Gabor filter, that is selective for elongated line structures with a preferred vertical orientation and a preferred width of four pixels.

In our experiments, we apply a bank of Gabor filters with six wavelengths equidistantly spaced on a logarithmic scale ($\lambda \in \{2(2^{\frac{i}{5}}) | i = 0 \dots 5\}$) and eight equidistant orientations ($\theta = \{\frac{\pi}{8}i | i = 0 \dots 7\}$) on segmented retinal fundus images of size 565×584 pixels and of size 605×700 pixels. In such images, the blood vessels have widths that vary from 1 to 7 pixels.

Fig. 2. A 2D Gabor function rendered as (a) a 2D intensity map and (b) a 3D surface, with the following parameter values: $\theta = 0$, $\lambda = 8$, $\gamma = 0.5$, $\sigma = 0.31\lambda$ and $\zeta = 0$. (c) 1D profile of the Gabor function along a horizontal cross section. The corresponding filter is selective for lines with preferred vertical orientation and a preferred width of $\lambda/2 = 4$ pixels.

We threshold the responses of Gabor filters at a given fraction t_1 ($0 \leq t_1 \leq 1$) of the maximum response of $g_{\lambda,\theta}(x,y)$ across all combinations of values (λ, θ) used and all positions (x,y) in the given image, and denote these thresholded responses by $|g_{\lambda,\theta}(x,y)|_{t_1}$. The choice of the threshold value depends on the contrast of the input images. For the binary segmented images that we use, a threshold value of $t_1 = 0.2$ proves sufficient to eliminate responses achieved on the background while preserving responses to features of interest. Fig. 3a illustrates the maximum value superposition of the thresholded responses of the concerned bank of Gabor filters obtained for the vascular bifurcation shown in Fig. 1b.

2.3. Configuration of a COSFIRE filter

A COSFIRE filter uses as input the responses of a number of Gabor filters, each characterized by a pair of parameter values (λ_i, θ_i) , around certain positions (ρ_i, ϕ_i) with respect to the center of the COSFIRE filter. A set of four parameter values $(\lambda_i, \theta_i, \rho_i, \phi_i)$ characterizes the properties of a contour part that is present in the specified area of interest ($\lambda_i/2$ represents the width, θ_i represents the orientation and (ρ_i, ϕ_i) represents the location in polar coordinates). In the following we explain how we obtain the parameter values of such contour parts around a given point of interest.

We consider the responses of the bank of Gabor filters along a circle of a given radius ρ around a point of interest (x,y) that is specified by a user, Fig. 3. In each position along that circle, we take the maximum of all responses across the possible values of (λ, θ) . The positions that have values greater than the corresponding values of the neighboring positions along an arc of angle $\pi/8$ are chosen as the points that characterize the dominant orientations

Fig. 3. (a) The gray-level of a pixel is the maximum value superposition of the thresholded responses ($t_1 = 0.2$) of a bank of Gabor filters at that position, $\max_{\lambda,\theta} |g_{\lambda,\theta}(x,y)|_{t_1}$. The cross marker indicates the location of the point of interest selected by a user, while the bright circle of a given radius ρ (here $\rho = 10$) indicates the locations considered in the analysis phase. (b) Values of the maximum value superposition of Gabor filter responses along the concerned circle. The labeled black dots in (a) mark the positions (relative to the center of the filter) at which the respective strongest Gabor filter responses are taken. These three positions correspond to the three local maxima in the plot in (b).

² We use $*$ to denote convolution.

³ <http://matlabserver.cs.rug.nl>.

around the point of interest. We determine the polar coordinates (ρ_j, ϕ_j) for such point with respect to the center of the filter. For each such location (ρ_j, ϕ_j) , we then consider all combinations of (λ, θ) for which the corresponding thresholded Gabor responses $|g_{\lambda, \theta}(x + \rho_j \cos \phi_j, y + \rho_j \sin \phi_j)|_{t_1}$ are greater than a fraction $t_2 = 0.75$ of the maximum of $|g_{\lambda, \theta}(x', y')|_{t_1}$ across the different combinations of values (λ, θ) used and across all locations in the given image. The threshold parameter t_2 implements a condition that the selected Gabor responses are significant and comparable to the strongest possible response. For each value θ that satisfies this condition, we consider a single value of λ , the one for which $|g_{\lambda, \theta}(x + \rho_j \cos \phi_j, y + \rho_j \sin \phi_j)|_{t_1}$ is the maximum of all responses across all values of λ . For each distinct pair of (λ, θ) and location (ρ_j, ϕ_j) , we obtain a tuple $(\lambda_i, \theta_i, \rho_i, \phi_i)$. Multiple tuples can thus be formed for the same location (ρ_j, ϕ_j) .

We denote by $S_f = \{(\lambda_i, \theta_i, \rho_i, \phi_i) | i = 1 \dots n_f\}$ the set of parameter value combinations, where n_f represents the number of contour parts which fulfill the above conditions. The subscript f stands for the prototype bifurcation. Every tuple in the set S_f specifies the parameters of some contour part in f .

For the point of interest shown in Fig. 3a and two given values of the radius ρ ($\rho \in \{0, 10\}$), the selection method described above results in the following set:

$$S_f = \left\{ \begin{array}{l} (\lambda_1 = 8\sqrt{2}, \theta_1 = 5\pi/8, \rho_1 = 0, \phi_1 = 0), \\ (\lambda_2 = 4\sqrt{2}, \theta_2 = 5\pi/8, \rho_2 = 10, \phi_2 = 0.3316), \\ (\lambda_3 = 4, \theta_3 = \pi/4, \rho_3 = 10, \phi_3 = 2.4260), \\ (\lambda_4 = 4, \theta_4 = 3\pi/8, \rho_4 = 10, \phi_4 = 2.4260), \\ (\lambda_5 = 4\sqrt{2}, \theta_5 = 5\pi/8, \rho_5 = 10, \phi_5 = 3.7001), \\ (\lambda_6 = 4\sqrt{2}, \theta_6 = 3\pi/4, \rho_6 = 10, \phi_6 = 3.7001) \end{array} \right\}$$

The second tuple in the above set S_f , $(\lambda_2 = 4\sqrt{2}, \theta_2 = 5\pi/8, \rho_2 = 10, \phi_2 = 0.3316)$, for instance, describes a contour part with a width of $\lambda_2/2 = 2.83$ pixels and an orientation of $\theta_2 = 5\pi/8$ that can be detected by a Gabor filter with preferred wavelength of $\lambda_2 = 4\sqrt{2}$ pixels and preferred orientation of $\theta_2 = 5\pi/8$, at a position of $\rho_2 = 10$ pixels to the north east, $\phi_2 = 0.3316$, of the point of interest; this location is marked by the label 'a' in Fig. 3. This selection is the result of the presence of a diagonally oriented blood vessel to the north east from the center of the prototype bifurcation that is used for the configuration of the COSFIRE filter.

2.4. Blurring and shifting Gabor filter responses

The above analysis of the given prototype bifurcation f indicates that this pattern produces six strong responses $g_{\lambda_i, \theta_i}(x, y)$ of Gabor filters with parameters (λ_i, θ_i) in the corresponding positions with polar coordinates (ρ_i, ϕ_i) with respect to the center of the COSFIRE filter. Next, we use these responses to compute the output of the COSFIRE filter. Since the concerned responses are in different positions (ρ_i, ϕ_i) with respect to the filter center, we first shift them appropriately so that they come together in the filter center. The COSFIRE filter output can then be evaluated as a pixel-wise multi-variate function of the shifted Gabor filter responses.

Before these shift operations, we blur the Gabor filter responses in order to allow for some tolerance in the position of the respective contour parts. We define the blurring operation as the computation of maximum value of the weighted responses of a Gabor filter. For weighting we use a Gaussian function $G_{\hat{\sigma}}(x, y)$, the standard deviation $\hat{\sigma}$ of which is a linear function of the distance ρ from the center of the COSFIRE filter: $\hat{\sigma} = \hat{\sigma}_0 + \alpha\rho$. Here we use $\hat{\sigma}_0 = 0.67$ and $\alpha = 0.1$. The choice of the linear function that we use to determine the standard deviation $\hat{\sigma}$ of the blurring function is explained in Section 4.

Next, we shift the blurred responses of each selected Gabor filter (λ_i, θ_i) by a distance ρ_i in the direction opposite to ϕ_i . In polar coordinates, the shift vector is specified by $(\rho_i, \phi_i + \pi)$, while in cartesian coordinates it is $(\Delta x_i, \Delta y_i)$ where $x_i = -\rho_i \cos \phi_i$ and $y_i = -\rho_i \sin \phi_i$. We denote by $s_{\lambda_i, \theta_i, \rho_i, \phi_i}(x, y)$ the blurred and shifted thresholded response of the Gabor filter that is specified by the i th tuple $(\lambda_i, \theta_i, \rho_i, \phi_i)$ in the set S_f :

$$s_{\lambda_i, \theta_i, \rho_i, \phi_i}(x, y) \stackrel{\text{def}}{=} \max_{x', y'} \{ |g_{\lambda_i, \theta_i}(x - x' - \Delta x_i, y - y' - \Delta y_i)|_{t_1} G_{\hat{\sigma}}(x', y') \} \quad (3)$$

where $-\hat{\sigma} \leq x', y' \leq \hat{\sigma}$.

Fig. 4 illustrates the blurring and shifting operations for this COSFIRE filter, for an input pattern that is cropped from the central region of the image in Fig. 1a. For each tuple in the configured set S_f we first compute the thresholded responses of the corresponding Gabor filters and then we blur and shift these responses accordingly.

2.5. COSFIRE filter response

We define the response $r_{S_f}(x, y)$ of a COSFIRE filter as the weighted geometric mean of all the blurred and shifted thresholded responses of Gabor filters $s_{\lambda_i, \theta_i, \rho_i, \phi_i}(x, y)$ that correspond to the properties of the contour parts described by set S_f :

$$r_{S_f}(x, y) \stackrel{\text{def}}{=} \left| \left(\prod_{i=1}^{|S_f|} (s_{\lambda_i, \theta_i, \rho_i, \phi_i}(x, y))^{\omega_i} \right)^{1/\sum_{i=1}^{|S_f|} \omega_i} \right|_{t_3} \quad (4)$$

$$\omega_i = \exp\left(\frac{-\rho_i^2}{2\hat{\sigma}^2}\right), \quad \hat{\sigma} = \sqrt{\frac{-\rho_{\max}^2}{2 \ln 0.5}}, \quad \rho_{\max} = \max_{i \in \{1, \dots, |S_f|\}} \{\rho_i\}$$

where $|\cdot|_{t_3}$ stands for thresholding the response at a fraction t_3 ($0 \leq t_3 \leq 1$) of its maximum across all image coordinates (x, y) . The input contribution of s -quantities decreases with an increasing value of the corresponding parameter ρ . Here, we use a value of the standard deviation $\hat{\sigma}$ that is computed as a function of the maximum value $\rho_{\max}$ of the given set of ρ values. We make this choice in order to achieve a maximum value $\omega = 1$ of the weights in the center (for $\rho = 0$), and a minimum value $\omega = 0.5$ in the periphery (for $\rho = \rho_{\max}$).

Fig. 4 shows the output of a COSFIRE filter, which is defined as the weighted geometric mean of six blurred and shifted images from the thresholded responses of five Gabor filters. Here, the maximum response is reached in the center of the prototype bifurcation that was used to configure this COSFIRE filter and the other three local maxima points correspond to bifurcations that are similar to the prototype bifurcation.

2.6. Tolerance to rotation, scale and reflection

In the following we provide details on how we achieve tolerance to rotation, scale and reflection.

We achieve rotation and scale tolerance by manipulating the set of parameter values in S_f , rather than by computing them from the responses to rotated and resized versions of the prototype pattern. Using the set S_f that defines the concerned filter, we form a new set $\mathfrak{R}_{\psi, v}(S_f)$ as follows:

$$\mathfrak{R}_{\psi, v}(S_f) \stackrel{\text{def}}{=} \{ (v\lambda_i, \theta_i + \psi, v\rho_i, \phi_i + \psi) | (\lambda_i, \theta_i, \rho_i, \phi_i) \in S_f \} \quad (5)$$

For each tuple $(\lambda_i, \theta_i, \rho_i, \phi_i)$ in the original filter S_f that describes a certain local contour part, we provide a counterpart tuple $(v\lambda_i, \theta_i + \psi, v\rho_i, \phi_i + \psi)$ in the new set $\mathfrak{R}_{\psi, v}(S_f)$. The preferred orientation of the concerned contour part and its polar angle position with respect to the center of the filter are offset by an angle ψ rel-

Fig. 4. (a) Part of the segmented retinal image shown in Fig. 1a. The enlaid inlay images show (top) the enlarged bifurcation encircled in the given image and (bottom) the structure of the COSFIRE filter that is configured by this prototype bifurcation. This COSFIRE filter is trained to detect the local spatial arrangement of six contour parts. The ellipses illustrate the orientations and wavelengths of the selected Gabor filters, and the bright blobs are intensity maps of 2D Gaussian functions that are used to blur the responses of the corresponding Gabor filters. The blurred responses are then shifted by the corresponding vectors. (b) Each contour part of the prototype pattern is detected by a Gabor filter with a given preferred wavelength λ_i and orientation θ_i . Two of these parts ($i = \{2, 5\}$) are detected by the same Gabor filter. (c) We then blur the thresholded response (here at $t_1 = 0.2$) of each concerned Gabor filter $|g_{\lambda_i, \theta_i}(x, y)|_{t_1}$ and subsequently shift the resulting blurred image by a polar coordinate vector $(\rho_i, \phi_i + \pi)$. (d) Finally, we obtain the output of the COSFIRE filter (here $t_3 = 0$) by computing the weighted geometric mean of all the blurred and shifted Gabor filter responses $s_{\lambda_i, \theta_i, \rho_i, \phi_i}(x, y)$. This COSFIRE filter gives local maximum responses in four points; the point with the strongest response corresponds to the prototype bifurcation and the other three points correspond to three bifurcations that are similar to the prototype bifurcation.

ative to the values of the corresponding parameters of the original tuple. Moreover, the width of the concerned contour part and its distance to the center of the filter are scaled by a factor v relative to the values of the corresponding parameters of the original tuple.

A rotation- and scale-tolerant response is then achieved by taking the maximum value of the responses of filters that are obtained with different values of the parameters ψ and v :

$$\hat{r}_{S_f}(x, y) \stackrel{\text{def}}{=} \max_{\psi \in \Psi, v \in \Upsilon} \{r_{\mathfrak{R}_{\psi, v}(S_f)}(x, y)\} \quad (6)$$

where Ψ is a set of n_ψ equidistant orientations defined as $\Psi = \{\frac{2\pi}{n_\psi} i | 0 \leq i < n_\psi\}$ and Υ is a set of v scale factors equidistant on a logarithmic scale defined as $\Upsilon = \{2^{\frac{i}{v}} | i \in \mathbb{Z}\}$. According to Eq. 6 a COSFIRE filter will produce the same response for local patterns that are versions of each other, obtained by rotation at discrete angles $\psi \in \Psi$ and resizing by given scale factors $v \in \Upsilon$. As to the response of the filter to patterns that are rotated at angles of intermediate values between those in Ψ , it depends on the orientation selectivity of the filter that is influenced by the orientation bandwidth of the involved Gabor filters and by the value of the parameter α , mentioned above. For $\alpha = 0.1$ that we use, $n_\psi = 16$ equidistant preferred orientations ensure sufficient response for any orientation of the local prototype pattern that is used to configure the COSFIRE filter.

As to reflection tolerance, we first form a new set $\hat{S}_f$ from the set S_f as follows:

$$\hat{S}_f \stackrel{\text{def}}{=} \{(\lambda_i, \pi - \theta_i, \rho_i, \pi - \phi_i) | \forall (\lambda_i, \theta_i, \rho_i, \phi_i) \in S_f\}. \quad (7)$$

The new filter, which is defined by the set $\hat{S}_f$, is selective for a reflected version of the prototype pattern f about the y -axis.

Finally, a combined rotation-, scale-, and reflection-tolerant response is computed as the maximum value of the rotation- and scale-tolerant responses of the filters S_f and $\hat{S}_f$ that are obtained with different values of the parameters ψ and v :

$$\bar{r}_{S_f}(x, y) \stackrel{\text{def}}{=} \max\{\hat{r}_{S_f}(x, y), \hat{r}_{\hat{S}_f}(x, y)\} \quad (8)$$

3. Experimental results

We use the DRIVE (Staal et al., 2004) and the STARE (Hoover et al., 2000) data sets of retinal fundus images to evaluate the performance of the COSFIRE filters by quantifying their effectiveness in detecting vessel features.

3.1. Data sets and ground truth

The DRIVE data set, which was obtained from a screening programme of diabetic retinopathy in the Netherlands, comprises 40 color images each of size 565×584 pixels. The STARE data set contains 20 retinal color images each of size 605×700 pixels, ten of which are of patients with no pathology and the other ten contain pathology.

These data sets are mainly used for the evaluation of algorithms for segmentation of the vessel tree. For this reason, next to the original photographic images the data sets also include the corresponding manually segmented binary images. The ground truth⁴ data, which comprises the coordinates of bifurcations and crossovers of the manually segmented retinal images⁵ was defined by the authors of this paper.

Fig. 5a and b show the grayscale version of the color retinal image with filename 40_training.tif and its segmentation in blood ves-

sels and background, respectively, which are both taken from the DRIVE data set (Staal et al., 2004). Fig. 5b contains 101 blood vessel features, shown encircled, which present Y- or T-form bifurcations or crossovers. Fig. 5d illustrates the superposition of the thresholded superimposed responses ($t_1 = 0.2$) of the bank of Gabor filters applied to the manually segmented image shown in Fig. 5b.

3.2. Configuration of COSFIRE filters

We configure COSFIRE filters in an iterative mode. In the first iteration, we use the prototype bifurcation f_1 illustrated in Fig. 1 to configure a COSFIRE filter denoted by S_{f_1} with three values of the radius parameter ρ ($\rho \in \{0, 4, 10\}$). Fig. 6f illustrates the structure of the filter S_{f_1} .

We then apply filter S_{f_1} to the same training image and show the obtained results in Fig. 7. We set the value of its threshold parameter $t_3(S_{f_1})$ to a fraction that produces the largest number of correctly detected bifurcations and no false positives. For COSFIRE filter S_{f_1} this criterium is satisfied for $t_3(S_{f_1}) = 0.39$. The encircled regions⁶ are centered on the local maxima of the filter response and if two such regions overlap by more than 75%, only the one with the stronger response is shown.

Without provisions for rotation and scale tolerance ($\Psi = \{0\}$, $\Upsilon = \{0\}$) COSFIRE filter S_{f_1} detects five vascular bifurcations, one of which is the prototype bifurcation that was used to configure this filter, Fig. 7a. When rotation tolerance is introduced ($\Psi = \{\frac{\pi}{8} i | i = 0 \dots 15\}$, $\Upsilon = \{0\}$), the number of correctly detected bifurcations is increased to 38, Fig. 7b. With the addition of scale tolerance ($\Psi = \{\frac{\pi}{8} i | i = 0 \dots 15\}$, $\Upsilon = \{-1, 0, 1\}$), filter S_{f_1} correctly detects 62 bifurcations, Fig. 7c. Finally, a total of 85 (out of 101) bifurcations are correctly detected when the filter is applied in rotation-, scale- and reflection-tolerant mode, Fig. 7d.

This high number of detected features illustrates the strong generalization capability of our approach because 84.16% of the features of interest are detected by a single COSFIRE filter. Notable is the fact that for the selected threshold $t_3(S_{f_1}) = 0.39$ the filter does not produce any false positive responses, which means that this result is achieved at precision of 100%. Fig. 7e–h show the features that are detected by the concerned COSFIRE filter rendered as enlarged and isolated patterns. Each gray dot indicates the location at which filter S_{f_1} achieves a local maximum response. Qualitatively, the indicated locations closely match the real branching points of interest.

In the second iteration of the training process, we randomly choose one of the bifurcations, which we denote by f_2 , that has not been detected by filter S_{f_1} and use it to configure a second COSFIRE filter S_{f_2} . With this second filter we detect 82 features of interest of which 70 coincide with the features detected by the first filter S_{f_1} and 12 are newly detected features ($t_3(S_{f_2}) = 0.21$). Merging the responses of both filters results in the detection of 97 distinct bifurcations.

We repeat this procedure of configuring filters using features that have not been detected by the previously trained filters until all the vessel features in the training image are detected. In this case, a set of five filters that are configured by the prototype bifurcations shown in Fig. 6a–e proves sufficient to detect all 101 retinal features in the concerned training image. An important aspect of this training procedure is that the values of the threshold parameters $t_3(S_{f_i})$ are chosen in such a way to produce a recall of 100% and a precision of 100%⁷ for the training retinal image.

⁶ The radius of the circle is the sum of the maximum value of the radial parameter ρ and blur radius used at this value of ρ .

⁷ Recall is the percentage of true bifurcations or crossovers that are successfully detected. Precision is the percentage of correct bifurcations or crossovers from all local maximum filter responses that exceed the corresponding t_3 threshold values.

⁴ The ground truth data can be downloaded from the following website: http://www.cs.rug.nl/imaging/databases/retina_database.

⁵ Named in DRIVE *_manual1.gif, and named in STARE *.ah.ppm.

Fig. 5. Example of a retinal fundus image from the DRIVE data set. (a) Original image (of size 565×584 pixels) with filename 40_training.tif. (b) The manual binary segmentation of vessels and background, also available in DRIVE. The typical widths of blood vessels vary between 1 and 7 pixels. This range of width values determines our choice of the set Λ of wavelength values used in the bank of Gabor filters. The circles surround Y- and T-formed vessel bifurcations and crossings. (c–d) Superposition of the responses of a bank of symmetric Gabor filters with a threshold (c) $t_1 = 0$ and (d) $t_1 = 0.2$.

Fig. 6. (a–e, k–o) A set of ten prototype bifurcations and (f–j, p–t) the structures of the corresponding ten COSFIRE filters. These bifurcations are all taken from the same retinal image with filename 40_training.tif. The following are the learned threshold values: $t_3(S_{f_1}) = 0.39$, $t_3(S_{f_2}) = 0.21$, $t_3(S_{f_3}) = 0.36$, $t_3(S_{f_4}) = 0.37$, $t_3(S_{f_5}) = 0.33$, $t_3(S_{f_6}) = 0.19$, $t_3(S_{f_7}) = 0.33$, $t_3(S_{f_8}) = 0.27$, $t_3(S_{f_9}) = 0.34$, and $t_3(S_{f_{10}}) = 0.32$.

3.3. Performance evaluation

We evaluate the effectiveness of the above five COSFIRE filters, which were configured from bifurcations selected from a single retinal image, on the entire data set of 40 manually segmented retinal images taken from the DRIVE data set. For this data set and for the determined values of the threshold parameters $t_3(S_{f_i})$ of the

corresponding filters we achieve a total recall R of 97.38% and a total precision P of 95.75%. Changing the values of the corresponding parameters $t_3(S_{f_i})$ yields different performance results: P increases and R decreases with increasing values of $t_3(S_{f_i})$. For each COSFIRE filter we add to (or subtract from) the corresponding learned threshold value $t_3(S_{f_i})$ the same offset value in steps of 0.01. With the referred five COSFIRE filters, the harmonic mean ($2PR/(P + R)$)

Fig. 7. (a) Results of applying the filter S_{f_1} to the training retinal image (40_manual1.gif) in different modes. The number of detected true positive (TP) features increases as the filter achieves tolerance to geometric transformations: (a,e) non-tolerant (TP = 5), (b,f) rotation-tolerant (TP = 38), (c,g) rotation- and scale-tolerant (TP = 62), and (d,h) rotation-, scale- and reflection-tolerant (TP = 85). (e–f) Enlargement of the detected features in the corresponding retinal images. The gray dots indicate the positions at which the COSFIRE filter achieves local maximum responses. The surrounding circles correspond to the area of support of the concerned COSFIRE filter.

of the precision and recall reaches a maximum at a recall R of 98.26% and a precision P of 94.98% when each value of the threshold parameter $t_3(S_{f_i})$ is offset by the same value of -0.01 from the corresponding learned threshold value, Fig. 8b.

3.4. Effects of the number of COSFIRE filters

In the above experiments we made no assumptions on the required number of COSFIRE filters. The performance results may, however, change with a different number of such filters. We

Fig. 8. (a) The plot illustrates the maximum harmonic mean achieved by using different number of COSFIRE filters. The best performance is achieved with only six COSFIRE filters for a maximum harmonic mean of 97.20%. This point is indicated by the filled-in circle. (b) Precision-recall plots obtained with five and six COSFIRE filters. For each plot the threshold values of parameters $t_3(S_{f_i})$ are varied by adding the same offset value, ranging between -0.05 to $+0.05$ in intervals of 0.01 , to the corresponding learned threshold values. The precision P increases and the recall R decreases with an increasing offset value. The harmonic mean of precision and recall reaches a maximum at $R = 97.81\%$ and $P = 96.60\%$ for six filters and at $R = 98.26\%$ and $P = 94.98\%$ for five filters. These points are indicated by a filled-in circle and a filled-in square marker, respectively.

consider this aspect and configure more COSFIRE filters as follows. First, we use the same training retinal image and apply to it the above set of five COSFIRE filters, but this time with the value of their respective threshold parameters $t_3(S_{f_i})$ offset by $+0.1$. For this offset value the COSFIRE filters become more selective and achieve a recall of 81.19% at a precision of 100% for the training retinal image. Then, we use the iterative training procedure described above to configure more COSFIRE filters until all the features of interest are detected in the training retinal image. It turns out that by configuring another five COSFIRE filters, Fig. 6k–t, and applying them together with the first five filters to the concerned image we achieve a recall of 100% at a precision of 100%.

We evaluate the effectiveness of the set of 10 COSFIRE filters by executing 10 experiments on the same data set of 40 retinal images. In the first experiment we only apply the first COSFIRE filter S_{f_1} and in the subsequent experiments we increment the number of COSFIRE filters one by one, in the same order that they are configured, Fig. 6. For each experiment we compute the maximum harmonic mean and show it in the plot in Fig. 8a. The maximum harmonic mean is achieved with only six COSFIRE filters for a recall of 97.81% at a precision of 96.60%, Fig. 8b. This result is achieved when the learned value of each threshold parameter $t_3(S_{f_i})$ is offset by the same value of $+0.03$. In Fig. 8b we show the corresponding precision-recall plot for these six filters together with the one for five filters.

3.5. Effects of the training data

We achieve the above performance results by applying six COSFIRE filters that were configured by using bifurcations that we selected from a single retinal image. Here we test whether the training retinal image that we use has an effect on the performance of the COSFIRE filters. For this purpose we repeat the entire experimental procedure for another two training retinal images.

Table 1

Performance results for separate sets of COSFIRE filters that are configured by using bifurcations selected from different training retinal images. Although the number of resulting COSFIRE filters may vary, the random selection of the training retinal image does not effect the global performance results. The harmonic mean H of recall R and precision P is comparable across the three experiments.

Exp. no.	Filename of training image	No. of COSFIRE filters	R (%)	P (%)	H (%)
1	40_manual1.gif	6	97.81	96.60	97.20
2	21_manual1.gif	5	98.46	96.66	97.58
3	38_manual1.gif	5	97.36	97.57	97.46
Average performance			97.88	96.94	97.41

For the first of the two new experiments we use the training retinal image with filename 21_manual1.gif that we randomly choose from the DRIVE data set. In this case, we achieve a maximum harmonic mean for a recall of 98.46% and a precision of 96.66% for the entire data set of 40 images with only five COSFIRE filters. For the second experiment, in which we use the training retinal image with filename 38_manual1.gif, it turns out that the best performance is also achieved with five COSFIRE filters: recall of 97.36% at a precision of 97.57%.

Our conclusion is that the selection of the training retinal image does not effect the overall performance of the COSFIRE filters. Table 1 shows the comparable performance results that we achieve for the three experiments.

3.6. Evaluating the generalization ability of COSFIRE filters

We use the STARE data set to evaluate the generalization ability of the six COSFIRE filters that we configured above. We apply the concerned six filters and evaluate their performance by varying the originally learned corresponding threshold values $t_3(S_{f_i})$ by given offsets.

For the 20 manually segmented retinal images of the STARE data set we reach a maximum harmonic mean at a recall of 97.83% and a precision of 95.64% when the threshold values $t_3(S_{f_i})$ are offset by +0.02. For the same offset value of +0.03 which contributed to the maximum harmonic mean that we achieved for the DRIVE data set, we achieve a recall of 97.32% at a precision of 96.04% for the STARE data set.

We carry out further experiments on binary retinal images that are automatically segmented by a program. We use the state-of-the-art algorithm⁸ proposed by Soares et al. (2006) to automatically segment the fundus images of the DRIVE data set. We randomly select 10 binary images⁹ that are automatically segmented with the concerned algorithm and use them to evaluate the generalization ability of the same six COSFIRE filters. Fig. 9b illustrates an example of one vessel tree that is automatically extracted from the original retinal image shown in Fig. 9a. For these 10 images and for the same six COSFIRE filters we achieve a maximum harmonic mean at a recall of 97.02% and a precision of 96.53% when the threshold values $t_3(S_{f_i})$ are also offset by a value of +0.03.

Similar to other algorithms, the automatic segmentation technique that we use suffers from insufficient robustness to preserve the connectedness of certain bifurcations. This problem is typically addressed by applying some morphological operations, such as closing. However, such enhancements do not consider the orientation of the involved contours before filling the gaps, and thus they

usually introduce artefacts. Bifurcation detection approaches that are based on the skeleton of the vessel tree, such as the ones proposed in (Martinez-Perez et al., 2002; Chanwimaluang and Guoliang, 2003; Eunhwa and Kyungho, 2006; Bhuiyan et al., 2007; Ardizzone et al., 2008; Aibinu et al., 2010; Calvo et al., 2011) fail to detect incomplete bifurcations. Here, we do not apply any post-processing techniques to the resulting binary image that is obtained by the concerned segmentation algorithm because the COSFIRE filters are robust to such incomplete bifurcations. This robustness is attributable to the tolerance that we allow in the position of the involved contour parts. Fig. 9c shows few examples of incomplete bifurcations that are nevertheless correctly detected by the COSFIRE filters.

The results that we achieve for the STARE images and for the automatically segmented DRIVE images are similar to the best results that we achieve on the DRIVE data set of manually segmented images. These results demonstrate the generalization ability of the six COSFIRE filters that we configured on a single manually segmented retinal image that we selected from the DRIVE data set.

4. Discussion

In our work we are concerned with the shape-recognition performance of the proposed COSFIRE approach and we choose to isolate this from low contrast effects that come with color/grayscale retinal images. We evaluate the performance of the COSFIRE filters that we use on manually segmented retinal images provided in the DRIVE (Staal et al., 2004) and in the STARE (Hoover et al., 2000) data sets but also on segmented retinal images that are automatically produced by the state-of-the-art algorithm that was introduced by Soares et al. (2006).

We showed that by using a single training retinal image we could configure a small set of COSFIRE filters, in this case six, and subsequently use them to effectively detect the vessel features in segmented retinal images. We demonstrated that the training retinal image that we randomly chose did not effect the performance of the resulting COSFIRE filters. We also showed that the COSFIRE filters have strong generalization ability as they achieved comparable performance across three data sets. As to the localization accuracy, we showed some qualitative results but did not compute it quantitatively because the ground truth was not provided by medical experts. Nevertheless, the precision and the localization accuracy can be improved by performing additional analysis of the features that are detected by the COSFIRE filters.

The performance results (harmonic mean of 97.20%: recall of 97.81% and precision of 96.60%) that we achieve on the manually segmented images of the DRIVE data set outperform the ones (harmonic mean of 96.83%: recall of 98.52% and precision of 95.19%) that we obtained with a preliminary method (Azzopardi and Petkov, 2011). Moreover, the results that we report are comparable to the ones obtained by other studies but they do not report results for the entire data sets of DRIVE and STARE. For instance, Bhuiyan et al. (2007) report a recall of 95.82% on a small data set of five retinal images only. Aibinu et al. (2010) report a total recall of 98.35% and a total precision of 95.22% on a small set of five retinal images taken from the STARE data set. Other studies (Ali et al., 1999; Shen et al., 2001; Martinez-Perez et al., 2002; Chanwimaluang and Guoliang, 2003; Tsai et al., 2004; Eunhwa and Kyungho, 2006; Ardizzone et al., 2008; Calvo et al., 2011) that also investigated the detection of vessel features do not provide results on the DRIVE and on the STARE data sets.

In the iterative training process we start by randomly selecting a typical bifurcation to configure the first filter and in every subsequent iteration we configure a filter by a bifurcation that is randomly selected from the bifurcations that are not detected by the

⁸ The Matlab code of Soares et al. (2006) can be downloaded from <<http://sourceforge.net/apps/mediawiki/retinal/index.php?title=Software>>.

⁹ The segmented images that we use are produced from the color retinal images named: 02_test.tif, 04_test.tif, 07_test.tif, 09_test.tif, 10_test.tif, 12_test.tif, 13_test.tif, 16_test.tif, 18_test.tif, 19_test.tif.

Fig. 9. (a) Original retinal fundus image (of size 565×584 pixels) with filename 02_test.tif that is taken from the DRIVE data set. (b) The corresponding segmented image that is automatically obtained by the algorithm proposed by Soares et al. (2006). The encircled bifurcations that are shown enlarged in (c) are few examples of incomplete bifurcations that are correctly detected by the COSFIRE filters. The gray dots in (c) indicate the locations at which the COSFIRE filters achieve local maximum responses.

previously configured filters. The selection of a different order of prototype bifurcations may yield to more (or less) than six COSFIRE filters to achieve the same or similar performance. By systematically analyzing the orientation and scale statistics of given training bifurcations one may configure an optimal set of COSFIRE filters. Such an approach was applied by Wang et al. (2005) to select an optimal bank of Gabor filters for the recognition of characters.

The configuration of a COSFIRE filter models the spatial arrangement of dominant contour parts that lie along concentric circles of given radii around a specified point of interest. A COSFIRE filter becomes more selective with an increasing number of such circles. Here we use vascular bifurcations to configure COSFIRE filters that receive input from selected channels of a bank of symmetric Gabor filters. The prototype patterns and Gabor filters are, however, not intrinsic to the method. Elsewhere we show that COSFIRE filters can be configured by other types of prototype patterns (Azzopardi et al., 2012a). Moreover, we demonstrated that by using Mexican hat operators, rather than Gabor filters, we can effectively configure a contour operator that we call CORF (Azzopardi and Petkov, 2012b).

We implemented the proposed approach in Matlab¹⁰ and ran all experiments on a personal computer with a 2.3 GHz processor. We also made this application available on the internet.¹¹ The number of computations that is required to process a retinal image does not depend on the number of COSFIRE filters used. This is because multiple COSFIRE filters may share many computations. In practice, the computation of one blurred and shifted response (for the same values of the parameters λ , θ and ρ), for instance with $s_{\lambda,\theta,\rho,\phi=0}(x,y)$, is sufficient: the result of $s_{\lambda,\theta,\rho,\phi}(x,y)$ for any value of ϕ can be obtained from the result of the output of $s_{\lambda,\theta,\rho,\phi=0}(x,y)$ by appropriate shifting. Therefore, the number of computations required depend on the total number of combinations of values (λ, θ, ρ) involved in all the COSFIRE filters used. For six values of λ , eight values of θ and three values of ρ that we use to configure the COSFIRE filters it results in a maximum of 144 blurring operations. The remaining computations for shifting and computing the responses of the COSFIRE filters are negligible. The six COSFIRE filters that we use involve a total number of 41 unique combinations of (λ, θ, ρ) and they take less than 50 s to process one retinal image of size 565×584 pixels. We note that the implementation that we use here is based on sequential processing. The COSFIRE approach can, however, be easily implemented in a parallel mode as most of the computations are independent of each other.

The multivariate function that we use to combine the responses of Gabor filters is weighted geometric mean. In future work, we plan to experiment with other functions. The way we determine the standard deviation of the blurring function is inspired by neurophysiological evidence that the average diameter of receptive fields¹² of V4 neurons increases with the eccentricity (Gattass et al., 1988).

The COSFIRE filters that we use differ from other bifurcation detection approaches in two main aspects. First, in comparison to skeleton-based approaches our method is more robust for the detection of incomplete junctions that are typically incorrectly produced by automatic segmentation algorithms. Skeleton-based approaches also involve some pre-processing techniques, such as morphological operations and skeletonization, which are not required by the COSFIRE approach. Second, the model-based approaches suggested in the literature (Ali et al., 1999; Shen et al., 2001; Tsai et al., 2004) design a fixed model with *a priori* knowledge and pre-define it in the implementation. This is also the case for skeleton-based approaches that use a pre-defined set of template kernels. On the contrary, a COSFIRE filter is trainable as it is configured with any local pattern that is specified by a user. Thus, the COSFIRE approach is more versatile and can be used to detect patterns other than bifurcations and crossovers.

In future work we will evaluate the COSFIRE filters on grayscale retinal images and we will extend this work to create a descriptor of certain properties, such as angle measurement, of the detected bifurcations. Another direction for future research is to extend this approach to 3D COSFIRE filters that can be applied, for instance, to tubular organ registration and bifurcation detection in X-ray computed tomography (CT) medical images.

5. Conclusions

We demonstrated that the trainable COSFIRE filters that we use are an effective means to automatically detect vascular bifurcations in manually and automatically segmented retinal fundus images. We achieve an average recall of 97.88% at an average precision of 96.94% on the DRIVE data set of 40 manually segmented retinal images, a recall of 97.32% at a precision of 96.04% on the STARE data set of 20 manually segmented retinal images, and a recall of 97.02% at a precision of 96.53% on 10 automatically segmented retinal images from the DRIVE data set.

¹⁰ Matlab scripts for the configuration and application of COSFIRE filters can be downloaded from <http://matlabserver.cs.rug.nl/>.

¹¹ <http://matlabserver.cs.rug.nl/RetinalVascularBifurcations>.

¹² In neurophysiology a receptive field refers to an area in the visual field which provides input to a given neuron. Its mathematical counterpart is the support of an operator.

The COSFIRE filters are versatile detectors of contour related features because they can be trained with any local contour prototype pattern and are subsequently able to detect patterns that are identical or similar to the prototype pattern. Furthermore, they are conceptually simple and easy to implement: the filter output is computed as the weighted geometric mean of blurred and shifted Gabor filter responses.

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References

- Abramoff, M., Garvin, M., Sonka, M., 2010. Retinal imaging and image analysis. *IEEE Rev. Biomed. Eng.* 3, 169–208. <http://dx.doi.org/10.1109/RBME.2010.2084567>, ISSN 1937-3333.
- Aibinu, A.M., Iqbal, M.I., Shafie, A.A., Salami, M.J.E., Nilsson, M., 2010. Vascular intersection detection in retina fundus images using a new hybrid approach. *Comput. Biological Med.* 40 (1), 81–89. <http://dx.doi.org/10.1016/j.combiomed.2009.11.004>, ISSN 0010-4825.
- Ali, C., Hong, S., Turner, J., Tanenbaum, H., Roysam, B., 1999. Rapid automated tracing and feature extraction from retinal fundus images using direct exploratory algorithms. *IEEE Trans. Inform. Technol. Biomed.* 3, 125–138.
- Ardizzone, E., Pirrone, R., Gambino, O., Radosta, S., 2008. Blood vessels and feature points detection on retinal images. In: *Engineering in Medicine and Biology Society, EMBS 2008. 30th Annual Internat. Conf. IEEE*, pp. 2246–2249. <http://dx.doi.org/10.1109/IEMBS.2008.4649643>, ISSN 1557-170X.
- Azzopardi, G., Petkov, N., 2011. Detection of retinal vascular bifurcations by trainable V4-like filters. In: Real, P., Diaz-Pernil, D., Molina-Abril, H., Berciano, A., Kropatsch, W. (Eds.), *Computer Analysis of Images and Patterns. Proc. 14th Internat. Conf. CAIP 2011, Seville, Spain*, pp. 451–459. ISBN 978-3-642-23671-6.
- Azzopardi, G., Petkov, N., 2012a. Trainable COSFIRE filters for keypoint detection and pattern recognition. *IEEE Trans. Pattern Anal. Machine Intell.* (99), 1. <http://dx.doi.org/10.1109/TPAMI.2012.106>, ISSN 0162-8828.
- Azzopardi, G., Petkov, N., 2012b. A CORF computational model of a simple cell that relies on LGN input outperforms the Gabor function model. *Biological Cybernet.* 106 (3), 177–189. <http://dx.doi.org/10.1007/s00422-012-0486-6>, ISSN 0340-1200.
- Becker, D., Can, A., Turner, J., Tanenbaum, H., Roysam, B., 1998. Image processing algorithms for retinal montage synthesis, mapping, and real-time location determination. *IEEE Trans. Biomed. Eng.* 45 (1), 105–118. <http://dx.doi.org/10.1109/10.650362>, ISSN 0018-9294.
- Bevilacqua, V., Cambo, S., Cariello, L., Mastronardi, G., 2005. A combined method to detect retinal fundus features. In: *Proc. of European Conf. on Emergent Aspects of Clinical Data Analysis*, pp. 1–6.
- Bhuiyan, A., Nath, B., Chua, J., Ramamohanarao, K., 2007. Automatic detection of vascular bifurcations and crossovers from color retinal fundus images. In: *Third Internat. IEEE Conf. on Signal-Image Technologies and Internet-Based System (SITIS)*, pp. 711–718.
- Bodis-Wollner, I., Brannan, J., 1997. Hidden visual loss in optic neuropathy is revealed using Gabor patch contrast perimetry. *Clin. Neurosci.* 4 (5), 284–291, ISSN 1065-6766.
- Calvo, D., Ortega, M., Penedo, M.G., Rouco, J., 2011. Automatic detection and characterisation of retinal vessel tree bifurcations and crossovers in eye fundus images. *Comput. Methods Prog. Biomed.* 103 (1), 28–38. <http://dx.doi.org/10.1016/j.cmpb.2010.06.002>, ISSN 0169-2607.
- Chanwimaluang, T., Guoliang, F., 2003. An efficient blood vessel detection algorithm for retinal images using local entropy thresholding. In: *Proc. 2003 IEEE Internat. Symposium on Circuits and Systems (Cat. No. 03CH37430)* 5, pp. 21–25.
- Chapman, N., Dell'omo, G., Sartin, M., Witt, N., Hughes, A., Thom, S., Pedrinelli, R., 2002. Peripheral vascular disease is associated with abnormal arteriolar diameter relationships at bifurcations in the human retina. *Clin. Sci.* 103, 111–116.
- Chaudhuri, S., Chatterjee, S., Katz, N., Nelson, M., Goldbaum, M., 1989. Detection of blood-vessels in retinal images using tow-dimensional matched-filters. *IEEE Trans. Med. Imaging* 8 (3), 263–269. <http://dx.doi.org/10.1109/42.34715>, ISSN 0278-0062.
- Chen, Li, Xiang, Yang, Chen, Yaojie, Zhang, XiaoLong, 2011. Retinal image registration using bifurcation structures. In: *2011 18th IEEE Internat. Conf. on Image Processing (ICIP 2011)*, IEEE Signal Process. Soc., 11–14 Sept. 2011, Brussels, Belgium, pp. 2169–2172. ISBN 978-1-4577-1304-0.
- Daugman, J., 1985. Uncertainty relation for resolution in space, spatial-frequency, and orientation optimized by two dimensional visual cortical filters. *J. Opt. Soc. Amer. A – Opt. Image Sci. Vision* 2 (7), 1160–1169. <http://dx.doi.org/10.1364/JOSA-A.2.001160>, ISSN 0740-3232.
- Du, Xiaojun, Bui, T., 2010. Retinal image segmentation based on Mumford-Shah model and Gabor wavelet filter. In: *Proc. 2010 20th Internat. Conf. Pattern Recognition (ICPR 2010)*, IEEE Comput. Soc., Istanbul, Turkey, pp. 3384–3387. ISBN 978-0-7695-4109-9.
- Eunhwa, J., Kyungho, H., 2006. Automatic retinal vasculature structure tracing and vascular landmark extraction from human eye image. In: *Internat. Conf. on Hybrid Information Technology* 7.
- Frank, R., 2004. Diabetic retinopathy. *New Engl. J. Med.* 350 (1), 48–58. <http://dx.doi.org/10.1056/NEJMra021678>, ISSN 0028-4793.
- Fraz, M., Remagnino, P., Hoppe, A., Velastin, S., Uyyanonvara, B., Barman, S., 2011. A supervised method for retinal blood vessel segmentation using line strength, multiscale Gabor and morphological features. In: *2011 IEEE Internat. Conf. on Signal and Image Processing Applications (ICSIPA 2011)*, pp. 410–415, 16–18 November 2011, Kuala Lumpur, Malaysia. ISBN 978-1-4577-0243-3.
- Gattass, R., Sousa, A.P., Gross, C.G., 1988. Visuotopic organization and extent of V3 and V4 of the macaque. *J. Neurosci.* 8 (6), 1831–1845.
- Gheorghiu, E., Kingdom, F.A.A., 2009. Multiplication in curvature processing. *J. Vision* 9 (2), Article No. 23. <http://dx.doi.org/10.1167/9.2.23>.
- Grigorescu, S.E., Petkov, N., Kruijinga, P., 2002. Comparison of texture features based on Gabor filters. *IEEE Trans. Image Process.* 11 (10), 1160–1167. <http://dx.doi.org/10.1109/TIP.2002.804262>, ISSN 1057-7149.
- Grigorescu, C., Petkov, N., Westenberg, M.A., 2003a. The role of non-CRF inhibition in contour detection. *J. Comput. Graphics Visualiz. Comput. Vision (WSCG)* 11 (2), 197–204.
- Grigorescu, C., Petkov, N., Westenberg, M.A., 2003b. Contour detection based on nonclassical receptive field inhibition. *IEEE Trans. Image Process.* 12 (7), 729–739.
- Hoover, A., Kouznetsova, V., Goldbaum, M., 2000. Locating blood vessels in retinal images by piecewise threshold probing of a matched filter response. *IEEE Trans. Med. Imaging* 19 (3), 203–210. <http://dx.doi.org/10.1109/42.845178>, ISSN 0278-0062.
- Jiang, X., Mojon, D., 2003. Adaptive local thresholding by verification-based multithreshold probing with application to vessel detection in retinal images. *IEEE Trans. Pattern Anal. Machine Intell.* 25 (1), 131–137, ISSN 0162-8828.
- Kruijinga, P., Petkov, N., 1999. Non-linear operator for oriented texture. *IEEE Trans. Image Process.* 8 (10), 1395–1407.
- Martinez-Perez, M., Hughes, A., Stanton, A., Thom, S., Chapman, N., Bharath, A., Parker, K., 2002. Retinal vascular tree morphology: A semi-automatic quantification. *IEEE Trans. Biomed. Eng.* 49, 912–917.
- Mendonca, A.M., Campilho, A., 2006. Segmentation of retinal blood vessels by combining the detection of centerlines and morphological reconstruction. *IEEE Trans. Med. Imaging* 25 (9), 1200–1213. <http://dx.doi.org/10.1109/TMI.2006.879955>, ISSN 0278-0062.
- Moin, M., Tavakoli, H., Broumandnia, A., 2010. A new retinal vessel segmentation method using preprocessed Gabor and local binary patterns. In: *2010 6th Iranian Conf. on Machine Vision and Image Processing (MVIP)*, IEEE Iran Sect., Isfahan, Iran, 6 pp. ISBN 978-1-4244-9706-5.
- Muramatsu, C., Hayashi, Y., Sawada, A., Hatanaka, Y., Hara, T., Yamamoto, T., Fujita, H., 2009. Computerized detection of retinal nerve fiber layer defects in retinal fundus images by modified polar transformation and Gabor filtering. In: Dossel, O., Schlegel, W. (Eds.), *11th International Congress of the IUPEM. Medical Physics and Biomedical Engineering. World Congress 2009. Biomedical Engineering for Audiology, Ophthalmology, Emergency & Dental Medicine*, 7–12 Sept. 2009, Munich, Germany, pp. 124–126. ISBN 978-3-642-03890-7.
- Murray, C.D., 1926a. The physiological principle of minimum work applied to the angle of branching of arteries. *J. Gen. Physiol.* 9, 835–841.
- Murray, C.D., 1926b. The physiological principle of minimum work: I. The vascular system and the cost of blood volume. *Proc. Natl. Acad. Sci. USA* 12, 207–214.
- Niemeijer, M., Staal, J., van Ginneken, B., Loog, M., Abramoff, M., 2004. Comparative study of retinal vessel segmentation methods on a new publicly available database. In: *Proceedings of the SPIE – The International Society for Optical Engineering, Medical Imaging San Diego, CA, USA*, pp. 648–656.
- Ortega, M., Penedo, M.G., Rouco, J., Barreira, N., Carreira, M.J., 2009. Personal verification based on extraction and characterisation of retinal feature points. *J. Vision Lang. Comput.* 20 (2), 80–90. <http://dx.doi.org/10.1016/j.jvlc.2009.01.006>, ISSN 1045-926X.
- Parisi, V., Manni, G., Spadaro, M., Colacino, G., Restuccia, R., Marchi, S., Bucci, M., Pierelli, F., 1999. Correlation between morphological and functional retinal impairment in multiple sclerosis patients. *Invest. Ophthalmol. Vision Sci.* 40 (11), 2520–2527, ISSN 0146-0404.
- Pasupathy, A., Connor, C., 1999. Responses to contour features in macaque area V4. *J. Neurophysiol.* 82, 2490–2502.
- Pasupathy, A., Connor, C., 2001. Shape representation in area V4: position-specific tuning for boundary conformation. *J. Neurophysiol.* 86, 2505–2519.
- Pasupathy, A., Connor, C., 2002. Population coding of shape in area V4. *Nat. Neurosci.* 5, 1332–1338.
- Patton, N., Aslam, T., MacGillivray, T., Deary, I., Dhillon, B., Eikelboom, R., Yogesan, K., Constable, I., 2006. Retinal image analysis: concepts, applications and potential. *Prog. Retinal Eye Res.* 25, 99–127.
- Paulus, W., Schwarz, G., Werner, A., Lange, H., Bayer, A., Hofschuster, M., Muller, N., Zrenner, E., 1993. Impairment of retinal increment thresholds in Huntington's disease. *Annal. Neurol.* 34 (4), 574–578. <http://dx.doi.org/10.1002/ana.410340411>, ISSN 0364-5134.
- Petkov, N., 1995. Biologically motivated computationally intensive approaches to image pattern-recognition. *Future Gener. Comput. Systems* 11, 451–465.
- Petkov, N., Kruijinga, P., 1997. Computational models of visual neurons specialised in the detection of periodic and aperiodic oriented visual stimuli: bar and grating cells. *Biological Cybernet.* 76 (2), 83–96.

- Petkov, N., Westenberg, M.A., 2003. Suppression of contour perception by band-limited noise and its relation to non-classical receptive field inhibition. *Biological Cybernet.* 88 (10), 236–246.
- Li, Qin, You, J., Zhang, Lei, Bhattacharya, P., 2006. A multiscale approach to retinal vessel segmentation using Gabor filters and scale multiplication. In: 2006 IEEE Conf. Systems, Man, and Cybernetics, Taipei, Taiwan, pp. 3521–3527. ISBN 1-4244-0099-6.
- Rangayyan, R.M., Zhu, X., Ayres, F.J., Ells, A.L., 2010. Detection of the optic nerve head in fundus images of the retina with Gabor filters and phase portrait analysis. *J. Digital Imag.* 23 (4), 438–453. <http://dx.doi.org/10.1007/s10278-009-9261-1>, ISSN 0897-1889.
- Ricci, E., Perfetti, R., 2007. Retinal blood vessel segmentation using line operators and support vector classification. *IEEE Trans. Med. Imaging* 26 (10), 1357–1365. <http://dx.doi.org/10.1109/TMI.2007.898551>, ISSN 0278-0062.
- Selvathi, D., Lalitha Vaishnavi, P., 2011. Gabor wavelet based blood vessel segmentation in retinal images using kernel classifiers. In: Proc. 2011 Internat. Conf. on Signal Processing, Communication, Computing and Networking Technologies (ICSCCN 2011), Thuckafay, India, pp. 830–835. ISBN 978-1-61284-653-8.
- Shen, H., Roysam, B., Stewart, C., Turner, J., Tanenbaum, H., 2001. Optimal scheduling of tracing computations for real-time vascular landmark extraction from retinal fundus images. *IEEE Trans. Inform. Technol. Biomed.* 5 (1), 77–91, ISSN 1089-7771.
- Shen, H., Stewart, C., Roysam, B., Lin, G., Tanenbaum, H., 2003. Frame-rate spatial referencing based on invariant indexing and alignment with application to online retinal image registration. *IEEE Trans. Pattern Anal. Mach. Intell.* 25 (3), 379–384, ISSN 0162-8828.
- Sherman, T., 1981. On connecting large vessels to small – The meaning of Murray law. *J. Gen. Physiol.* 78, 431–453.
- Soares, J.V.B., Leandro, J.J.G., Cesar Jr., R.M., Jelinek, H.F., Cree, M.J., 2006. Retinal vessel segmentation using the 2-D Gabor wavelet and supervised classification. *IEEE Trans. Med. Imag.* 25 (9), 1214–1222. <http://dx.doi.org/10.1109/TMI.2006.879967>, ISSN 0278-0062.
- Staal, J., Abramoff, M., Niemeijer, M., Viergever, M., van Ginneken, B., 2004. Ridge-based vessel segmentation in color images of the retina. *IEEE Trans. Med. Imaging* 23, 501–509.
- Sun, H., Dul, M.W., Swanson, W.H., 2006. Linearity can account for the similarity among conventional, frequency-doubling, and Gabor-based perimetric tests in the glaucomatous macula. *Optometry Vision Sci.* 83 (7), 455–465, ISSN 1040-5488.
- Tsai, C., Stewart, C., Tanenbaum, H., Roysam, B., 2004. Model-based method for improving the accuracy and repeatability of estimating vascular bifurcations and crossovers from retinal fundus images. *IEEE Trans. Inform. Technol. Biomed.* 8, 122–130.
- Tso, M., Jampol, L., 1982. Path-physiology of hypertensive retinopathy. *Ophthalmology* 89, 1132–1145.
- Usman Akram, M., Tariq, A., Nasir, S., Khan, S., 2009. Gabor wavelet based vessel segmentation in retinal images. In: 2009 IEEE Symposium on Computational Intelligence for Image Processing (CIIP), 30 March–2 April 2009, Nashville, TN, USA, 4 pp. ISBN 978-1-4244-2760-4.
- Wang, X., Ding, X., Liu, C., 2005. Gabor filters-based feature extraction for character recognition. *Pattern Recognition* 38 (3), 369–379. <http://dx.doi.org/10.1016/j.patcog.2004.08.004>, ISSN 0031-3203.
- Yavuz, Z., Koumlse, C., 2010. Comparing 2D matched filter response and Gabor filter methods for vessel segmentation in retinal images. In: 2010 National Conf. on Electrical, Electronics and Computer Engineering (ELECO 2010), Bursa, Turkey, pp. 648–652. ISBN 978-1-4244-9588-7.
- Yavuz, Z., Kose, C., 2011. Retinal blood vessel segmentation using Gabor filter and top-hat transform. In: 2011 IEEE 19th Signal Processing and Communications Applications Conference (SIU 2011), Antalya, Turkey, pp. 546–549. ISBN 978-1-4577-0462-8.
- Zamir, M., Medeiros, J., Cunningham, T., 1979. Arterial bifurcations in the human retina. *J. Gen. Physiol.* 74 (4), 537–548.
- Zamir, M., Sinclair, P., Wonnacott, T., 1992. Relation between diameter and flow in major branches of the arch of the aorta. *J. Biomech.* 25 (11), 1303–1310. [http://dx.doi.org/10.1016/0021-9290\(92\)90285-9](http://dx.doi.org/10.1016/0021-9290(92)90285-9), ISSN 0021-9290.